Attorney Docket No.: 6443.500-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Hansen et al.
Serial No.: 10/699,338
Filed: October 31, 2003
For: Chemical Uncouplers for the Treatment of Obesity

Confirmation No.: 2536
Group Art Unit: 1614
Examiner: Kwon, Brian Yong S

PETITION TO RESTART TIME FOR RESPONSE TO A NON-FINAL OFFICE ACTION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants hereby petition to restart the time for response to the non-final Office Action that was issued in the above-identified application on March 20, 2008.

Applicants participate in the e-office action program offered by the US Patent and Trademark Office, which provides that all correspondence from the US Patent and Trademark Office is sent to Applicants electronically. Applicants do not receive any correspondence from the US Patent and Trademark Office by mail. Applicants are sent an automatic email notification from PAIR (PAIR_eOfficeAction@uspto.gov), which serves to inform Applicants about new outgoing correspondence.

According to PAIR the office action in the above-identified application had been issued on **March 20, 2008**. However, Applicants did not receive the email notification from PAIR until **May 6, 2008**.

Applicants did not receive the "Courtesy Reminder Post Card", which is typically mailed by the US Patent and Trademark Office 7 days after a new document has been posted on PAIR. There is no record on PAIR that such a postcard was mailed to the Applicants.

In support of this petition, enclosed are the following:

(1) Email notification from PAIR dated May 6, 2008, informing the Applicants that new correspondence had been issued in the above-identified application

(2) Print-out from PAIR evidencing lack of any record of the "Courtesy Reminder Post Card."

Accordingly, the undersigned respectfully requests that this petition be granted and the time for response to the non-final office action dated March 20, 2008, be reset taking into consideration the email dated May 6, 2008.

The applicants believe that no petition fee is due. However, please charge any additional fees, should they be required, to Deposit Account No. 141447.

Respectfully submitted,

Date: July 15, 2008

/ Rosemarie R. Wilk-Orescan, Reg. No. 45,220 /
Rosemarie R. Wilk-Orescan, Reg. No. 45,220
Novo Nordisk Inc.
Customer Number 23650
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To: nnipatent@novonordisk.com,KSHL@novonordisk.com,KISW@novonordisk.com
From: PAIR_eOfficeAction@uspto.gov
Cc: PAIR_eOfficeAction@uspto.gov
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May 06, 2008 06:34:35 AM

Dear PAIR Customer:

NOVO NORDISK, INC.
INTELLECTUAL PROPERTY DEPARTMENT
100 COLLEGE ROAD WEST
PRINCETON, NJ 08540
UNITED STATES

The following USPTO patent application(s) associated with your Customer Number, 23650 , have new outgoing correspondence. This correspondence is now available for viewing in Private PAIR. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

Application	Attorney Docket No.
10699338	6443.500-US

To view your correspondence online or update your email addresses, please visit us anytime at https://sportal.uspto.gov/secure/myportal/privatepair. If you have any questions, please email the Electronic Business Center (EBC) at EBC@uspto.gov or call 1-866-217-9197 during the following hours:

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ROOR/MEWS PROJECT #112
DOCKETED BY CSSZ 05/06/08

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,338	10/31/2003	Birgit Sehested Hansen	6443.500-US	2536

23650 7590 03/20/2008

NOVO NORDISK, INC.
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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
03/20/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nnipatent@novonordisk.com
KSHL@novonordisk.com
KISW@novonordisk.com

Office Action Summary	Application No.	Applicant(s)	
	10/699,338	HANSEN ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5-9,14,15 and 17* is/are pending in the application.

4a) Of the above claim(s) *8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5-7,14,15 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114.

2. Acknowledgement is made of applicant's filing of amendment/remarks on 12/21/2007. By the amendment, claims 2 and 17 have been amended and claims 1, 12, 13, 20 and 44-49 have been cancelled.

3. The rejection of claims 2, 5-7 and 14-15 under 35 USC 112, 1st paragraph, as containing subject matter which was not described in the specification is not maintained in light of the amendment filed 12/21/2007.

4. The rejection of claims 2, 5-7, 14-15 and 17 under 35 USC 112, first paragraph, as lacking enablement for treating various diseases conditions encompassed by the instant claims with the administration of compound of formula I is not maintained in light of the amendment filed 12/21/2007. However, the amendment changing the scope of the invention by reciting "endometrial cancer, breast cancer, prostate cancer and colon cancer" and formula III compounds in claim 2 necessitates a new ground of rejection in this Office Action.

5. The rejection of claims 2, 5-7, 14-15 and 17 under 35 USC 103(a) is maintained for the reasons of record. No arguments to the examiner's contentions have been present by applicant in Response filed 12/21/2007. In absence of applicant's argument explaining how the claims avoid the references or distinguish from them, the examiner maintains the rejection of record.

6. As discussed above, rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or

newly applied. They constitute the complete set of actions being applied to the instant application.

7. Claims 2, 5-7, 14-15 and 17 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 2, 14-15 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of increasing glucose utilization, treating diabetes or obesity and/or impaired glucose tolerance with the administration of the specific compound of the formula III, does not reasonably provide enablement for treating atherosclerosis, hypertension, dyslipidemia, coronary heart disease, gallbladder disease, osteoarthritis, endometrial cancer, breast cancer, prostate cancer and colon cancer with all compounds encompassed by the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are'. (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of

the art; (5) the breadth of the claims; (6) the amount .... of direction or guidance presented; (7) the presence or absence of working examples; and (81) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant invention relates to a method of treating a disease condition benefiting from an enhancement of mitochondrial respiration, namely obesity, atherosclerosis, hypertension, diabetes, type 2 diabetes, impaired glucose tolerance, dyslipidemia, coronary heart disease, gallbladder disease, osteoarthritis and cancer, by the administration of the claimed compound(s) represented by the formula I having a slope calculated from an equation or a pharmaceutically acceptable salt or solvate thereof.

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art are very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological Compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Affd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a biological compound is considered to be an unpredictable art and the physiological or pharmaceutical activity of treating "a disease condition benefiting from an enhancement of mitochondrial respiration..." is an unpredictable art.

The claims are very broad due to the vast number of possible diseases conditions that are described as being "a disease condition benefiting from an enhancement of mitochondrial

respiration" including "obesity, atherosclerosis, hypertension, diabetes, type 2 diabetes, impaired glucose tolerance, dyslipidemia, coronary heart disease, gallbladder disease, osteoarthritis, cancer, endometrial cancer, breast cancer, prostate cancer, colon cancer and the maintenance of a weight loss". Furthermore, the claims are further complicated by plethora of compounds having characteristic of "a slope value calculated from the equation", particularly compounds of the formula (III).

At the time of the invention was made, it was generally recognized in diabetes therapy art that the intensive blood-glucose control with anti-diabetic substantially decrease the risk of microvasuclar complications, such as retinopathy, neuropathy and nephropathy, but not macrovascular disease such as hypertension, atherosclerosis and cardiovascular outcomes (see Lancet, Vol. 352, Sept. 12, 1998).

Although some known chemical uncouplers that have activities in increasing the metabolic rate may be useful in treating obesity or diabetes, it is not known yet that a single underlying mechanism ties together all of the seemingly unrelated manifestation of the disease conditions encompassed (for example, atherosclerosis, hypertension, dyslipidemia, coronary heart disease, gallbladder disease, osteoarthritis, endometrial cancer, breast cancer, prostate cancer and colon cancer). There is no demonstrated correlation or sufficient evidence in the specification or incorporated by reference that increased glucose utilization would be able to treat all the diseases encompassed by the instant claims. Therefore, the skilled artisan would turn to undue amount of trial and error to find out which disease or condition would be response to the administration of sad compounds.

The specification discloses the effects of increased glucose utilization (Figures 1- 3) using the compounds that have a slope value calculated from an equation. However, the specification fails to provide how to use the invention commensurate in scope with these claims without undue amount of experimentation. As discussed in preceding comments, in the instant case, only a limited number of "a compound capable of increase glucose utilization" in vitro study is disclosed in the specification, thereby the specification fails to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The instant claims read on any compounds of formula III having "a slope value calculated from the equation", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

As discussed in preceding comments, to practice the instant invention to the claimed scope, applicant would have to (i) make or screen numerous potentially suitable compounds of the formula I characterized as "having a slope value calculated from the equation", (ii) undergo assays to find out which compounds are able to exert the desired pharmacological activity, and then (iii) extrapolate the test and result to the claimed therapeutic utility. In other words, the instant invention necessitates for the skilled artisan to undergo an exhaustive search for the embodiments suitable to practice the claimed invention.

Given the breadth, the disparate nature of compounds that is presently claimed, the highly unpredictable state of the art where many specific differences or different physicochemical properties are existed among unrelated structural compounds or even structurally related compounds, the limited number of working examples and the insufficient amount of guidance

present in the specification, one of ordinary skill in the art would have to undergo an undue amount of experimentation to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2, 14-15 and 17 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation "diabetes", and the claim also recites "type 2 diabetes" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 2, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticiapted by Tang et al. (US 5891917).

Tang discloses (E)-2-benzenesulfonyl-3-(3,5-di-tert-butyl-4-hydroxy-phenyl)acrylonitrile and (E)-3-(3,5-di-tert-butyl-4-hydroxy-phenyl)-2-(4-fluoro-benesulfonyl)-acrylonitrile which reads on the instant formula III compounds, as tyrosine kinase inhibitors, that is useful for the treatment of diseases mediated through HER2, EGFR, IGFR, KDR/FLK-1 and C-MET disorders including breast cancer, endometrial cancer, colorectal cancer, non-small cell lung cancer, gastric, ovarian adenocarcinomas, prostate cancer and diabetes (entire documents, especially columns 3-4; column 8, line 56 through column 9, line 11; column 9, lines 42-48; column 10, line 53 through column 11, line 7; column 10, line 56 through column 12, line 2; Examples 7, 18, 36, 66, 78 and 81).

With respect to the recitation of "increasing mitochondrial respiration" in the claims, when the same compound is administered to treat the same patient population, the mechanism of action of "increasing mitochondrial respiration" deems to be inherent to the referenced method. Therefore, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

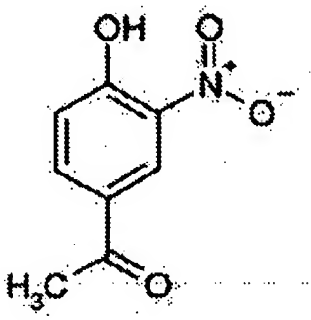
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 2, 5-7, 14-15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachynsky (US Patent 4,673,691, issue date: Jun. 16, 1987) in view of Batt et al. (US Patent 5,593,994, issue date: Jan. 14, 1997) and Rink et al. (US Patent 5,739,106, issue date: Apr. 14, 1998) as applied to claims 4-7. This rejection is analogous to the original rejection.

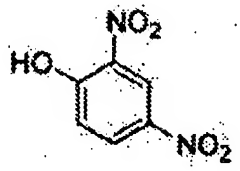
The instant claims are directed to a method comprising the administration of a compound of formula III having a slope calculated from an equation as defined in the claim. Further limitation include that the method is for treating a disorders, such as type II diabetes, obesity, atherosclerosis, hypertension, impaired glucose tolerance, dyslipidemia, coronary heart disease, gall bladder disease, osteoarthritis and endometrial cancer, breast cancer, prostate cancer and colon cancer in a patient.

A compound for the treatment is the elected species of 4-hydroxy-3-nitroacetophenone



having the following structure:

Bachynsky teaches a method of inducing weight loss in a patient comprising administering 2,4-dinitrophenol (DNP) (column 6, lines 20-22) having the following structure:



The prior art teaching differs from the instant invention in that (i) the prior art compound has a nitro group at position 4 whereas the compound of the instant invention has an aceto group at position 4 and (ii) the prior art does not disclose that the obese patient has type II diabetes. However, the base structure of the prior art compound 2,4-dinitrophenol is the same as the base

structure of 4-hydroxy-3-nitroacetophenone of the instant invention and the physiological activities are analogous. In addition, Batt et al. disclose compounds for treatment where the substitute groups on the benzene ring can be nitro or aceto (column 49, line 39). Therefore, the substitution of a nitro group with an aceto group on the benzene ring is obvious. One having ordinary skill in the art would have been motivated to substitute a nitro group of the prior art compound with an aceto group with the expectation that the substitution would not significantly alter the analogous properties of the compound due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055. With respect to the patient population for treatment in claims 4-7 where the patient who is obese is suffering from type II diabetes, Rink et al. disclose that obesity and type 2 diabetes are associated in both clinical and epidemiological studies (column 1, lines 29-31) and that weight reduction is often recommended as the first course of action for patients suffering from Type II diabetes (column 1, lines 42-45). Therefore, one having ordinary skill in the art would have been motivated to practice a weight reduction method of treatment to treat obese patient who is suffering from Type II diabetes.

Therefore, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the treatment of Bachynsky in view of Rink et al. with compound modifications in view of Batt et al. to result in the practice of the instant invention with a reasonable expectation of success.

The recitation of the compound having a slope calculated from an equation as defined in claims 2, 5-9 and 14-17 is merely a characterization of the compound and therefore does not limit the claims.

With respect to the recitation of "increasing mitochondrial respiration" in the claims, when the same compound is administered to treat the same patient population, the mechanism of action of "increasing mitochondrial respiration" is expectedly present.

Regarding the recitation of claim 14, since there is no extra active step in the method of treatment for conducting the Assay, the compound being a chemical uncoupler as defined is merely a characterization of the compound and therefore does not limit the claim.

Regarding the recitation of claim 15, since the nitro group of the prior art compound is the same nitro group of the instant compound, the fact that the nitro group is a cation is merely a characterization of the compound and therefore does not limit the claim.

12. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (US 5891917) in view of Tang et al. (US 6514981).

The teaching of Tang'917 has been discussed in above 35 USC 102(b) rejection.

Tang'981 teaches the use of tyrosine kinase inhibitor for the treatment of various disese conditions including obesity (column 40, line 48 and column 51, line 60) and diabetes, particularly type II diabetes (column 51, line 55 and lines 66-67; column 52, line 35).

The teaching of Tang'917 differs from the instant invention in the use of said compounds for the treatment of obese-type II diabetes. To incorporate such teaching into the teaching of Tang'917, would have been obvious in view of Tang'981 who teaches the utility of tyrosine kinase inhibitor in the treatment obesity and type II diabetes.

Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients

and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Conclusion

13. No Claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614

Notice of References Cited	Application/Control No. 10/699,338	Applicant(s)/Patent Under Reexamination HANSEN ET AL.	
	Examiner Brian-Yong S. Kwon	Art Unit 1614	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,225,346	05-2001	Tang et al.	514/523
*	B	US-5,891,917	04-1999	Tang et al.	514/604
*	C	US-5,935,993	08-1999	Tang et al.	514/445
*	D	US-5,789,427	08-1998	Chen et al.	514/352
*	E	US-5,773,476	06-1998	Chen et al.	514/620
*	F	US-6,596,878	07-2003	Chen et al.	548/371.7
*	G	US-2,365,981	12-1944	TINDALL JOHN B	568/946
*	H	US-6,514,981	02-2003	Tang et al.	514/267
*	I	US-6,465,507	10-2002	Tang et al.	514/265.1
*	J	US-6,680,335	01-2004	Tang, Peng Cho	514/414
*	K	US-6,689,806	02-2004	Tang et al.	514/418
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes

Application/Control No.	Applicant(s)/Patent under Reexamination	
10/699,338	HANSEN ET AL.	
Examiner	**Art Unit**	
Brian-Yong S. Kwon	1614	

SEARCHED			
Class	Subclass	Date	Examiner
updated	search notes	3/13/2008	BK

INTERFERENCE SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES (INCLUDING SEARCH STRATEGY)		
	DATE	EXMR
Updated: STN, EAST, NPL	3/13/2008	BK
Updated: Continuity data, inventor name search		

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:00:47 ON 11 MAR 2008

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                                                           ENTRY    SESSION
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L5           15 L3 NOT 7605-28-9/RN

=> focus
PROCESSING COMPLETED FOR L5
L6           15 FOCUS L5 1-

=> d ibib abs hitstr 1-15

L6   ANSWER 1 OF 15  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:          1997:134866  CAPLUS
DOCUMENT NUMBER:           126:139910
TITLE:                     Tyrphostin-like compounds for the treatment of cell
                           proliferative disorders or cell differentiation
                           disorders
INVENTOR(S):               Tang, Peng Cho; Sun, Li; Nematalla, Asaad S.; McMahon,
                           Gerald
PATENT ASSIGNEE(S):        Sugen, Inc., USA
SOURCE:                    PCT Int. Appl., 112 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:             Patent
LANGUAGE:                  English
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:

      PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
      -------------------  ----   --------    -----------------------  --------
      WO 9640629            A1    19961219    WO 1996-US10213          19960604
          W:  AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
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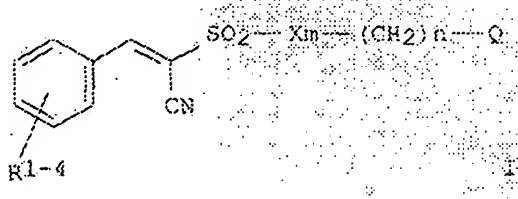
PRIORITY APPLN. INFO.: US 1995-480275 A 19950607
WO 1996-US10213 W 19960604
US 1997-957420 A1 19971024

OTHER SOURCE(S): MARPAT 126:139510

GI



I

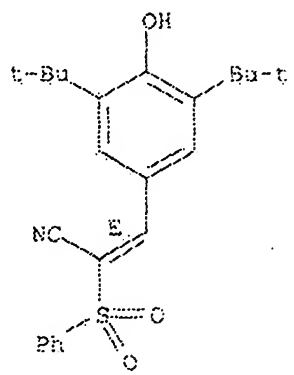
AB The present invention relates to compds. I (X = NH, -C(CN)=C, CH2CN; m = 0, 1; n = 0-3; Q = aryl, heteroaryl; R1-4 = halo, trihalo, Me, alkyl, alkoxy, hydroxy, H, nitro, cyano, amide, sulfonyl, sulfonamide, carboxy, carboxamide, amino), capable of modulating tyrosine signal transduction to prevent or treat cell proliferative disorders or cell differentiation disorders associated with particular tyrosine kinases by inhibiting one or more abnormal tyrosine kinase activities. (E)-3-(3,5-diisopropyl-4-hydroxyphenyl)-2-[(pyrid-2-yl)sulfonyl]acrylonitrile was prepared from a reaction mixture of 450 mg of 3,5-diisopropyl-4-hydroxylbenzaldehyde and 400 mg of 2-pyridinesulfonylacetonitrile in 10 mL ethanol. Examples were presented which illustrates the ability of the exemplary compds. to inhibit receptor tyrosine kinases, such as HER2 and/or EGFR.

IT **170449-05-5P 170449-06-6P 186582-17-2P**
186582-23-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tyrosine kinase inhibition by tyrphostin-like sulfonyl acetonitrile compds. for treatment of cell proliferative or cell differentiation disorders)

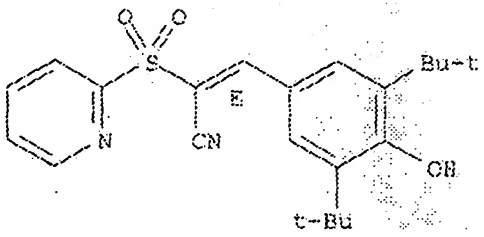
RN 170449-05-5 CAPLUS

CN 2-Propenenitrile, 3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2-(phenylsulfonyl)-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.

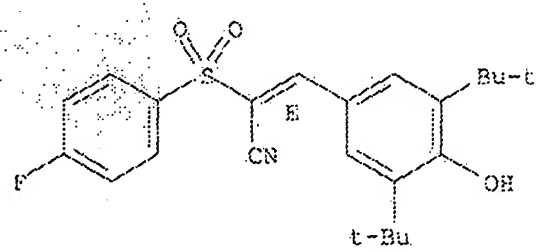


Example 87



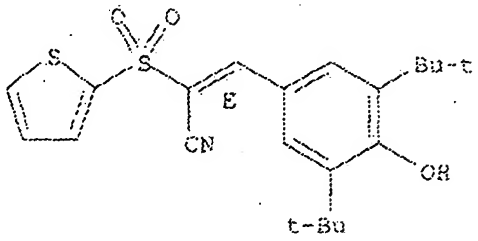
RN 186582-17-2 CAPLUS
CN 2-Propenenitrile, 3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2-[(4-fluorophenyl)sulfonyl]-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



RN 186582-23-0 CAPLUS
CN 2-Propenenitrile, 3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2-(2-thienylsulfonyl)-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



IT **170449-34-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(tyrosine kinase inhibition by tyrphostin-like sulfonyl acetonitrile compds. for treatment of cell proliferative or cell differentiation disorders)
RN 170449-34-0 CAPLUS
CN Acetonitrile, (2-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)

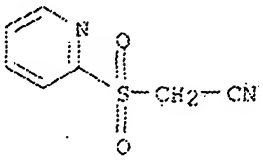
L6 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:534888 CAPLUS
DOCUMENT NUMBER: 129:156926
TITLE: Methods and compositions using receptor tyrosine kinase inhibitors for inhibiting cell proliferative disorders, and inhibitor preparation
INVENTOR(S): Chen, Hui; Gazit, Aviv; Hirth, Klaus Peter; Mann, Elaina; Shawver, Laura K.; Tsai, Jianming; Tang, Peng Cho
PATENT ASSIGNEE(S): Sugen, Inc., USA; Yissum Research & Development Company of the Hebrew University of Jerusalem
SOURCE: U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 207,933, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5789427	A	19980804	US 1995-399967	19950307
US 5773476	A	19980630	US 1995-486775	19950607
US 6596878	B2	20030722	US 2001-953933	20010918
US 2004242684	A1	20041202	US 2003-602617	20030625
US 7217737	B2	20070515		

PRIORITY APPLN. INFO.:

US 1994-207933	B2 19940307
US 1995-399967	A1 19950307
US 1995-486775	A1 19950607
US 1998-70318	B1 19980429
US 2000-722149	B1 20001122
US 2001-953933	A3 20010918

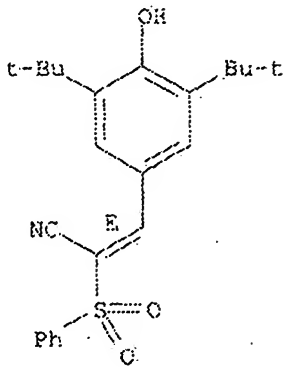
OTHER SOURCE(S): MARPAT 129:156926
AB The invention concerns compds. and their use to inhibit the activity of a receptor tyrosine kinase. The invention is preferably used to treat cell proliferative disorders, e.g. cancers characterized by over-activity or inappropriate activity HER2 or EGFR.
IT **170449-34-0**, 2-Pyridinesulfonylacetonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; recepter tyrosine kinase inhibitors, and preparation thereof, for inhibiting cell proliferative disorders)
RN 170449-34-0 CAPLUS
CN Acetonitrile, (2-pyridinylsulfonyl)- (9CI) (CA INDEX NAME)



IT **170449-05-5 170449-06-6 211299-44-4**

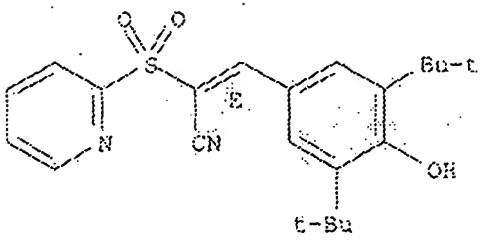
CN 2-Propenenitrile, 3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2-(phenylsulfonyl)-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



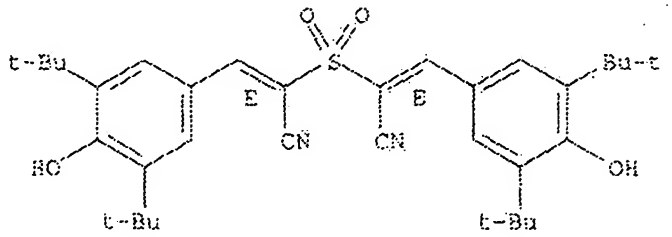
RN 170449-06-6 CAPLUS
CN 2-Propenenitrile, 3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-2-(2-pyridinylsulfonyl)-, (2E)- (CA INDEX NAME)

Double bond geometry as shown.



RN 211299-44-4 CAPLUS
CN 2-Propenenitrile, 2,2'-sulfonylbis[3-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-, (2E,2'E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

INVENTOR(S): Kleinman, Edward F.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp., Cont. of U.S. Ser. No. 489,689, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002013467	A1	20020131	US 2001-918099	20010730
US 2002147340	A1	20021010	US 2002-95218	20020311
US 6555538	B2	20030429		
US 2003203911	A1	20031030	US 2003-424451	20030428
PRIORITY APPLN. INFO.:			US 1999-117875P	P 19990129
			US 2000-489689	B1 20000124
			US 2001-918099	A1 20010730
			US 2002-95218	A3 20020311

OTHER SOURCE(S): MARPAT 136:151179
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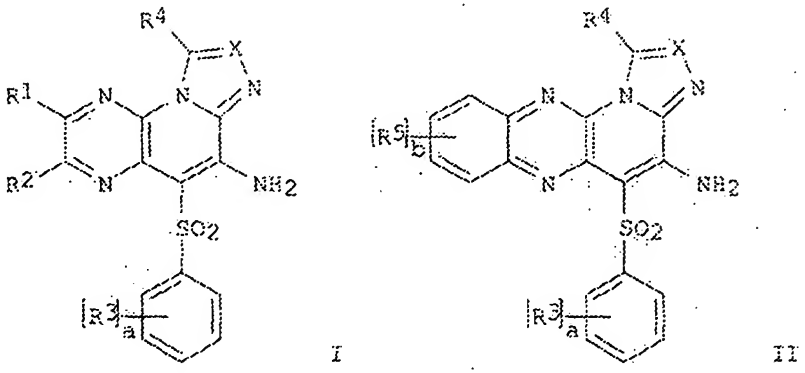
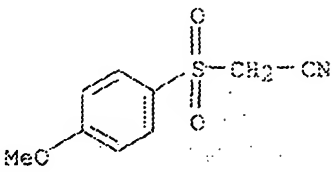


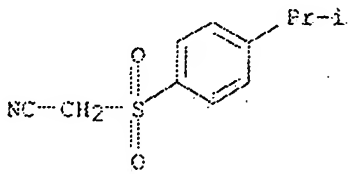
I II

AB The title compds. [I; a = 1-4; X = CH, N; R1, R2 = H, alkyl, CN, etc.; R3, R4 = H, halo, alkyl, etc.; or R1 and R2 may be taken together to form II (b = 1-4; R5 = H, halo, alkyl)], which are selective inhibitors of PDE4 and the production of TNF (no data), and as such are useful in the treatment of respiratory, allergic, rheumatoid, body weight regulation, inflammatory and central nervous system disorders such as asthma, chronic obstructive pulmonary disease, adult respiratory diseases syndrome, shock, fibrosis, pulmonary hypersensitivity, allergic rhinitis, atopic dermatitis, psoriasis, weight control, rheumatoid arthritis, cachexia, Crohn's disease, ulcerative colitis, arthritic conditions and other inflammatory diseases, depression, multi-infarct dementia and AIDS, were prepared Thus, reacting (4-methylbenzenesulfonyl)acetonitrile with 2,3-dichloropyrazine in the presence of K2CO3 in DMF (20%) followed by treatment of the resulting 2-pyrazineacetonitrile with 1-methylimidazole in DMF (37%) afforded I [X = CH; R1, R2 = H; R3 = 4-Me; R4 = H; a = 1].

IT **132276-87-0P 207853-59-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT



RN 207853-59-6 CAPLUS
CN Acetonitrile, [[4-(1-methylethyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

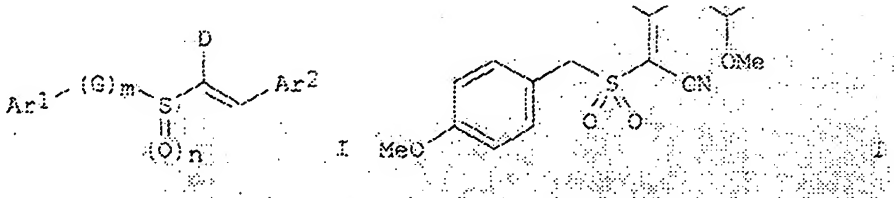


L6 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:156586 CAPLUS
DOCUMENT NUMBER: 148:238882
TITLE: Aryl vinyl sulfides, sulfones, sulfoxides and sulfonamides, derivatives thereof as antiproliferative agents and their preparation, pharmaceutical compositions and use in the treatment of proliferative diseases
INVENTOR(S): Reddy, E. Premkumar; Reddy, M. V. Ramana
PATENT ASSIGNEE(S): Temple University - Of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 168pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008016682	A2	20080207	WO 2007-US17266	20070801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-835146P P 20060802
GI

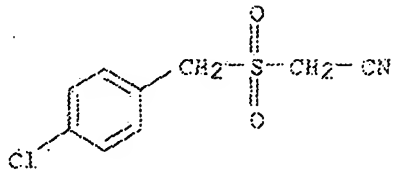


AB Compds. useful as antiproliferative agents, including, for example, anticancer agents, according to formula I, salts, antibody conjugates, pharmaceutical compns., methods of treatment, synthetic processes, and intermediates useful in such processes are provided. Compds. of formula I wherein Ar1 is (un)substituted phenyl; Ar2 is (un)substituted (hetero)aryl; D is CN, CONH2 and derivs., and NO2; G is C(R1)2 and NR1; R1 is H and C1-6 alkyl; m is 0 and 1, provided that if D is CN then m is 1; n is 0, 1, and 2, provided that if G is NR1 then n is 2; and salts thereof, are claimed. Example compound Ii was prepared by a general procedure (procedure given). All the invention compds. were evaluated for their antiproliferative activity. From the assay, it was determined that compound II exhibited IC50 value of 25 μM against DU145.

IT **175137-57-2P**
RL: PRPH (Prophetic); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prophetic intermediate; preparation of aryl vinyl sulfides, sulfones, sulfoxides and sulfonamides and their derivs. as antiproliferative agents useful in the treatment of proliferative diseases)

RN 175137-57-2 CAPLUS

CN Acetonitrile, 2-[[(4-chlorophenyl)methyl]sulfonyl]- (CA INDEX NAME)



L6 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:894558 CAPLUS
DOCUMENT NUMBER: 145:293054
TITLE: Preparation of imidazo[1,2-a]pyridines as VEGFR-2 inhibitors for treating neoplasm
INVENTOR(S): Barda, David Anthony; Burkholder, Timothy Paul; Clayton, Joshua Ryan; Hao, Yan; Heath, Perry Clark; Henry, James Robert; Knobeloch, John Monte; Mendel, David; Mclean, Johnathan Alexander; Remick, David Michael; Rempala, Mark Edward; Wang, Zhao-Qing; Yip, Yvonne Yee Mai; Zhong, Boyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 153pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

AU 2006216710	A1	20060831	AU 2006-216710		20060223
CA 2599124	A1	20060831	CA 2006-2599124		20060223
IN 2007KN02929	A	20070914	IN 2007-KN2929		20070810
KR 2007099029	A	20071008	KR 2007-719338		20070823
MX 200710326	A	20071016	MX 2007-10326		20070823
CN 101128461	A	20080220	CN 2006-80006004		20070824
NO 2007004666	A	20071109	NO 2007-4666		20070913
PRIORITY APPLN. INFO.:			US 2005-655981P	P	20050224
			WO 2006-US6283	W	20060223

OTHER SOURCE(S): MARPAT 145:293054
GI

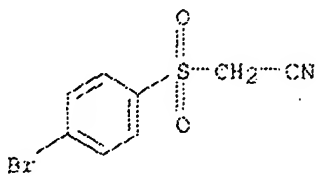
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is related to imidazopyridines I [R1 = (un)substituted 2-pyridonyl, Ph, thiophenl, pyrazolyl, etc.; R2, R3 = H, alkyl optionally substituted with OH; R4 = (un)substituted thiazolyl, pyridinyl, Ph; R5 = CONHR6, OC(:O)NHR6, NHCOCH2R6, NHCONHR6, C(:S)NHR6; ; X = (CH2)n; n = 0-4 for R5 = OC(:O)NHR6, NHCOCH2R6, NHCONHR6; n = 1-4 for R5 = CONHR6, C(:S)NHR6; R6 = (un)substituted tetrahydrobenzothiazolyl, Ph, pyridinyl, isoxazolyl, etc.], and their pharmaceutically acceptable salts, that are inhibitors of VEGFR-2 and methods of using them. Thus, reacting [4-[7-(4-methylsulfonylphenyl)imidazo[1,2-a]pyridin-3-yl]benzyl]amine (preparation given) with 3-trifluoromethylphenyl isocyanate gave imidazopyridine II in 66% yield. III demonstrated in vitro inhibition of against cell-based KDR autophosphorylation (IC50 = 42 nM). III displayed antitumor activity in PC-3 prostate tumor xenografts. I are useful as angiogenesis inhibitors and antitumor agents.

IT **126891-45-0**, (4-Bromophenylsulfonyl)acetonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of imidazo[1,2-a]pyridines as VEGFR-2 inhibitors for treating neoplasm)

RN 126891-45-0 CAPLUS

CN Acetonitrile, 2-[(4-bromophenyl)sulfonyl]- (CA INDEX NAME)



DOCUMENT NUMBER: 143:460024
TITLE: Indole derivatives as chemical uncouplers, their preparation, pharmaceutical compositions, and use in treatment of obesity and related conditions
INVENTOR(S): Olesen, Preben Houlberg; Rohlweg, Rolf
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105785	A2	20051110	WO 2005-EP52017	20050503
WO 2005105785	A3	20060119		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1758856	A2	20070307	EP 2005-743128	20050503
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007536344	T	20071213	JP 2007-512190	20050503

PRIORITY APPLN. INFO.: DK 2004-708 A 20040504
WO 2005-EP52017 W 20050503

OTHER SOURCE(S): CASREACT 143:460024; MARPAT 143:460024
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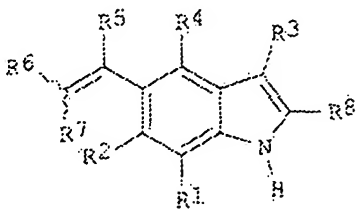

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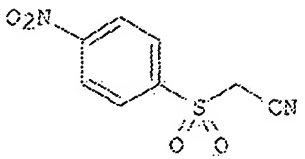

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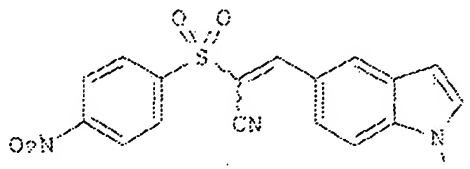
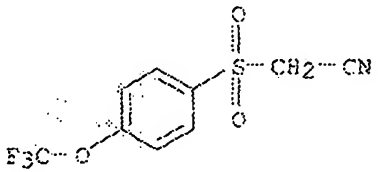


alkylamino, (un)substituted alkyl, (un)substituted aryl, (un)substituted heteroaryl, etc.; R5 is H, halo, nitro, cyano, alkyl, alkenyl, alkynyl, alkoxy, or alkylamino; R6 is 4-pyridinium radical, alkyl, alkenyl, alkynyl, carbonyloxy, carbonylamino, etc.; R7 is R or cyano, provided that if R7 is H, then R6 is a 4-pyridinium radical, or R6 and R7, together with the carbon atom to which they are attached, may form a 4-(dicyanomethylene)dihydrophenyl moiety; and R8 is selected from H, halo, nitro, cyano, (un)substituted haloalkyl, (un)substituted alkoxy, (un)substituted alkylamino, (un)substituted alkyl, (un)substituted aryl, (un)substituted heteroaryl, etc. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound of formula I, as well as to the use of the compns. in the treatment of obesity and related conditions. Chloroacetonitrile was substituted with 4-nitrothiophenol followed by oxidation to give sulfonylacetonitrile II. Knoevenagel condensation of II with 5-formylindole resulted in the formation of indolylacrylonitrile III. The compds. of the invention act as chemical uncouplers (no data) useful in the treatment of obesity and related conditions.

IT **217186-16-8**, {[4-(Trifluoromethoxy)benzene]sulfonyl}acetonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of indole derivs. as chemical uncouplers for treatment of obesity and related conditions)

RN 217186-16-8 CAPLUS

CN Acetonitrile, {[4-(trifluoromethoxy)phenyl]sulfonyl}- (9CI) (CA INDEX NAME)



L6 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:490349 CAPLUS

DOCUMENT NUMBER: 143:43677

TITLE: Sulfinyl- and sulfonylphenols as chemical uncouplers, their preparation and use for the treatment of obesity

INVENTOR(S): Olesen, Preben Houlberg

PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.

SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXKD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051900	A1	20050609	WO 2004-DK302	20040504

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

SN, TD, TG

EP 1689707	A1	20060816	EP 2004-730959	20040504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007512262	T	20070517	JP 2006-540162	20040504
US 2007004799	A1	20070104	US 2006-439857	20060524
PRIORITY APPLN. INFO.:			DK 2003-1736	A 20031125
			US 2003-526041P	P 20031201
			WO 2004-DK302	W 20040504

OTHER SOURCE(S): CASREACT 143:43677; MARPAT 143:43677
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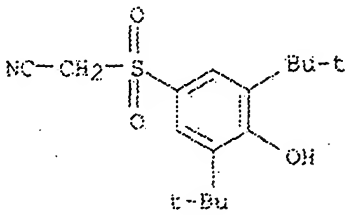
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a group of novel sulfinyl- and sulfonylphenols I, which are potent chemical uncouplers. In compds. I, R1 and R2 are independently selected from H, nitro, cyano, halo, alkyl, alkenyl, etc.; R3 is substituted alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy, or haloalkoxy; Y is S(O) or S(O)2; and X is a bond or O, including pharmaceutically acceptable salts, solvates and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. containing one or more compds., including I, as active ingredients, as well as to the use of the compns. for the treatment of obesity, prevention of weight gain, or the maintenance of weight loss. Alkylation of 2,6-di-tert-butyl-4-mercaptophenol with 4-chlorobenzyl chloride resulted in the formation of sulfide II. II was oxidized with H2O2 to give sulfonylphenol III, or with 3-chloroperoxybenzoic acid to give the corresponding sulfinylphenol. The compds. of the invention have been found to be potent chemical uncouplers (no data).

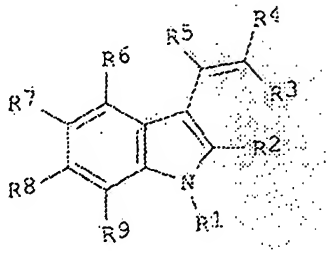
IT **797036-11-4P**, (3,5-Di-tert-butyl-4-hydroxybenzenesulfonyl)acetonitrile
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of sulfinyl- and sulfonylphenols for the treatment of obesity)

RN 797036-11-4 CAPLUS

CN Acetonitrile, [[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]sulfonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



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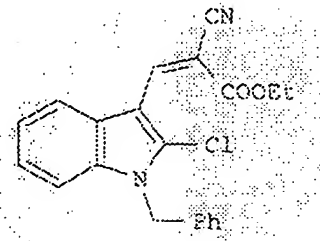


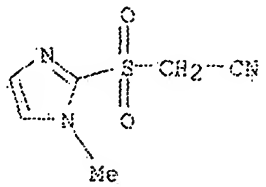
II

AB The title compds. [I; R1 = C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; R2 = halo, C1-6 alkyl, PhCH2, etc.; R3, R4 = H, CN, COOPh, etc.; R5 = H, C1-6 alkyl; R6-R9 = H, NO2, NH2, etc.], useful in treating epilepsy, senile dementia, Parkinson's disease, Huntington's Chorea, pain or deficiency of mental and motoric performance seen after conditions of brain ischemia, were prepared and formulated. Thus, reaction of 1-benzyl-2-chloroindole-3-carbaldehyde with Et 2-cyanoacetate in the presence of Et3N in EtOH afforded II which showed IC50 of 2.2 μM against PI-hydrolysis in BHK 570 cells expressing mGluR1α receptors.

IT **175137-63-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of indolyl compds. for treatment of diseases in the central nervous system related to the metabotropic glutamate receptor system)

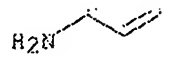
RN 175137-63-0 CAPLUS

CN Acetonitrile, [(1-methyl-1H-imidazol-2-yl)sulfonyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1946:16196 CAPLUS
DOCUMENT NUMBER: 40:16196
ORIGINAL REFERENCE NO.: 40:3126a-b
TITLE: Chloronitroalkanes
INVENTOR(S): Tindall, John B.
PATENT ASSIGNEE(S): Commercial Solvents Corp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2365981		19441226	US 1941-423765	19411220



L6 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1946:9981 CAPLUS
DOCUMENT NUMBER: 40:9981
ORIGINAL REFERENCE NO.: 40:1807a-h
TITLE: Chemotherapeutic agents of the sulfone type. I. Sulfones containing a p-aminophenyl group
AUTHOR(S): Walker, James
CORPORATE SOURCE: Natl. Inst. for Med. Research, London
SOURCE: Journal of the Chemical Society (1945) 630-3
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 40:9981

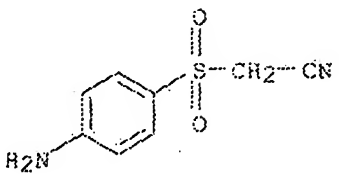
AB Compds. derived from p-H2NC6H4SO2Me by introduction of electroneg. substituents into the Me group with the object of increasing acidity or those which had acidic properties because of a phenolic HO group in close proximity to the SO2 group have been compared with p-H2NC6H4SO2NH2 for antibacterial activity. p-AcNHC6H4SO2Na (I) forms a hydrate with between 1.5 and 2 mols. of H2O; in this work 2 mols. were allowed in the amount of salt used. ClCH2CO2H (14.2 g.) and 37.2 g. I in NaOH, evaporated to dryness and the acid liberated with HCl, give 32 g. of the Ac derivative, m. 216-17°, of p-aminophenylsulfonylacetic acid (II), m. 164-5° (decomposition); the Ac derivative was hydrolyzed with 12% HCl by refluxing 0.5 h.; 3.55 g. yielded 2.3 g. of II. I (15.4 g.) and 4.8 cc. ClCH2Ac in 100 cc. 90% EtOH, refluxed 7 h., give 11.4 g. of the Ac derivative, with 1/3 mol. H2O, m. 91-3°, of p-aminophenylsulfonylacetone (III), m. 131-2° (7.2 g. from hydrolysis of 11.3 g. of Ac derivative). I (35 g.) and 13.3 g. of ClCH2CN in 70 cc. 75% aqueous EtOH, refluxed 17 h., give 31 g. of the Ac derivative, m. 263-4° (from 20% aqueous C5H5N), of p-aminophenylsulfonylacetonitrile (IV), m. 122-3° (17 g. from 23.8 g. Ac derivative on refluxing with 250 cc. 3 N HCl and 50 cc. EtOH for 40 min.). IV (8 g.) in 40 cc. dioxane and 10 cc. EtOH, saturated with dry HCl at 0° and allowed to stand at 0° for 14 days, the solvent and HCl removed in vacuo at room temperature, and the residue allowed to stand with 100 cc. 10% EtOH-NH3 at 37° for 5 days, gives p-aminophenylsulfonylacetamidine-HCl (V), decomps. about 265°. I (10.28 g.) and 6.9 g. Et2NC2H4Cl.HCl in 60 cc. H2O, refluxed 5 h., give about 5.6 g. of the Ac derivative, with 1 mol. of H2O, m. 94-6°, of 2-diethylamino-1-(p-aminophenylsulfonyl)ethane-HCl (VI), m. 186°. HO(CH2)2Cl (43.6 g.), 95 cc. Et2NH, and 3 cc. MeOH, kept at room temperature for 48 h. and refluxed 16 h., give 46.3 g. of Et2N(CH2)3OH, b28 85-8°; this yields 47.8 g. of Et2N(CH2)3Cl (VII), b15 65-70°. VII (10 g.) (neutralized with N HCl) and 18 g. I, refluxed 12 h. and the sirup hydrolyzed with 12% HCl, give 11.6 g. of 3-diethylamino-1-(p-aminophenylsulfonyl)propane, analyzed as the sulfate, m. 200°. p-C6H4O2 (4.32 g.) in 100 cc. hot H2O, treated with a warm solution of 10.3 g. I in 70 cc. H2O containing 41 cc. N HCl, gives 12.1 g. of the Ac derivative, m. 273°, of 2-(p-aminophenylsulfonyl)hydroquinone (VIII), m. 176-7°. Toluquinone (4.1 g.) and the acid from 8.6 g. I in H2O give 9.74 g. of the Ac derivative, m. 237-9°, of 5(?)-(p-

the solubility in H2O of the NH2 compds. rapidly diminishes. p-[illegible] p-MeC6H4SO2H give a quant. yield of 2-(p-tolylsulfonyl)hydroquinone, m. 211-12°. The following pKa values were determined: II 2.8, III 10.2, IV 10.6, VIII 8.4. The in vitro antibacterial activities of the NH2 compds. are reported. The activity of p-H2NC6H4SO2Me is comparable with that of p-H2NC6H4SO2NH2 and none of II-VI showed greater activity, although 4 of these 6 were somewhat more active than p-H2NC6H4SO2NH2 against hemolytic streptococci. The products from quinones showed high in vitro activity against a variety of pathogenic bacteria and, in vivo, local application in mice disclosed marked activity against infection with an organism of the gas gangrene group.

IT **797036-00-1P**, Acetonitrile, sulfanilyl-
RL: PREP (Preparation)
(preparation of)

RN 797036-00-1 CAPLUS

CN Acetonitrile, [(4-aminophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1946:2062 CAPLUS

DOCUMENT NUMBER: 40:2062

ORIGINAL REFERENCE NO.: 40:321i,322a-i,323a-d

TITLE: Synthesis of aminosulfones

AUTHOR(S): Goldberg, Alan A.; Besly, Donald M.

CORPORATE SOURCE: Ward, Blenkinsop & Co. Ltd., Bradford-on-Avon, Wilts, UK

SOURCE: Journal of the Chemical Society (1945) 566-71
CODEN: JCSOA9; ISSN: 0368-1769

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 40:2062

AB A possible synthesis of (p-aminophenylsulfonyl)alkanecarboxylic acids (which would be expected to be less toxic than (4-H2NC6H4)2SO2) consists in the condensation of p-AcNHC6H4SO2Cl with the Na derivative of AcCH2CO2Et or CH2(CO2Et)2, followed by acid hydrolysis of the product; however, the hydrolysis effects rupture of the C-S bond, with the formation of p-H2NC6H4SO3H. Anhydrous p-AcNHC6H4SO2Na (44.2 g.), 24.4 g. ClCH2CO2Et, and a trace of Cu in 300 cc. xylene, refluxed 5 h., give 40 g. of the Ac derivative (I), m. 122-4°, of Et (p-aminophenylsulfonyl)acetate (II), m. 112-14°; the HCl salt of II results in 18.5-g. yield from 20 g. I in 200 cc. saturated anhydrous EtOH-HCl on refluxing 1.5 h.; II was prepared from the aqueous solution of the salt by addition of NaHCO3. I (57 g.) in 320 cc. 5 N HCl, refluxed 75 min., give 41 g. of the HCl salt, m. 214-16° (decomposition), of (p-aminophenylsulfonyl)acetic acid (III), m. 162-4°; the amide, m. 194-6°, is formed by shaking II and concentrated NH4OH for [illegible] h. o-AcNHC6H4SO2H (199 g.), 95 g. ClCH2CO2H in 600 cc. H2O and 400 cc. 5

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10/699,338 **Chemical uncouplers for the treatment of obesity**

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Transaction History

Date	Transaction Description
05-07-2008	Electronic Review
05-06-2008	Email Notification
03-20-2008	Mail Non-Final Rejection
03-17-2008	Non-Final Rejection
01-02-2008	Date Forwarded to Examiner
01-02-2008	Date Forwarded to Examiner
12-21-2007	Request for Continued Examination (RCE)
01-02-2008	DISPOSAL FOR A RCE/CPA/129 (express abandonment if CPA)
12-21-2007	Request for Extension of Time - Granted
12-21-2007	Workflow - Request for RCE - Begin
08-01-2007	Electronic Review
07-31-2007	Email Notification
07-31-2007	Mail Final Rejection (PTOL - 326)
07-23-2007	Final Rejection
05-17-2007	Date Forwarded to Examiner
05-14-2007	Response after Non-Final Action
05-14-2007	Request for Extension of Time - Granted
05-13-2007	Case Docketed to Examiner in GAU
02-17-2007	Case Docketed to Examiner in GAU
12-15-2006	Mail Non-Final Rejection
12-11-2006	Non-Final Rejection
06-01-2004	Information Disclosure Statement considered
11-21-2006	Date Forwarded to Examiner
11-10-2006	Response to Election / Restriction Filed